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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/148,973	09/04/1998	J.TIMOTHY GREENAMYRE	PC10023A	4263

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PFIZER INC
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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/148,973	GREENAMYRE ET AL.	
	Examiner	Art Unit	
	Mark Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's Declaration Under 37 CFR 1.132, filed on 2/20/2004 has been entered.

Status of the Claims

2. Currently claims 1-8 are pending. Claims 1-7 are newly rejected. Claim 8 is objected to.

Information Disclosure Statement

3. The information disclosure statement filed 1/30/2004 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered.

Withdrawn Rejections

4. The rejection of claims 1-3 and 5-7 under 35 U.S.C. 103(a) as being unpatentable over Arnold et al. (US 5,670,516) in view of Adams et al. (Principles of Neurology, on PTO-1449) is withdrawn.

5. The rejection of claims 1-3 and 5-7 under 35 U.S.C. 103(a) as being unpatentable over Stella et al (Annals of Neurology, 1996; of record) in view of Arnold et al. (US 5,670,516) and further in view of Adams et al. (Principles of Neurology, on PTO-1449) is withdrawn.

The aforementioned rejections under 35 U.S.C. § 103(a) were withdrawn over the showings, *in part*, found in the Declaration Under 37 CFR 1.132, filed 2/20/2004 by Frank Menniti, PhD (hereinafter Menniti Declaration), as discussed below.

Declaration Under 37 CFR 1.132

6. The Menniti Declaration, at p. 3-4, bridging paragraph 6, states that "one of skill in the art could not have known what effects administering an AMPA receptor antagonist could have on the serotonin-dopamine interactions in patients with L-dopa and whether such effects would, for example, offset or exacerbate the effects caused by the dopamine agonist therapy." This argument is persuasive insofar as it pertains to the rejection of claims 1-3 and 5-7 under 35 U.S.C. 103(a) as being unpatentable over Arnold et al. (US 5,670,516) in view of Adams et al. (Principles of Neurology), and therefore, said rejection is withdrawn (*but, see below* new rejection under 35 U.S.C 103(a)).

The Menniti Declaration, at pp. 4-5, para 8, states that because AMPA and NMDA receptors serve distinct physiological functions and antagonists for the two receptor classes have distinct physiological effects, the observation by Papa and Chase

("Stella" reference) that an NMDA receptor antagonist reduced dopamine agonist-induced dyskinesias would not have led to the deduction of the utility of an AMPA receptor antagonist to treat dopamine agonist-induced dyskinesias. This argument is persuasive, and therefore, the rejection of claims 1-3 and 5-7 under 35 U.S.C. 103(a) as being unpatentable over Stella et al (Annals of Neurology, 1996; of record) in view of Arnold et al. (US 5,670,516) and further in view of Adams et al. (Principles of Neurology, on PTO-1449) is withdrawn.

The Menniti Declaration, at p. 4, para 7, states that the claimed invention's limitation that AMPA antagonists *inhibit* dopamine agonist induced dyskinesia was unanticipated and contraindicated at the time of the publication of Arnold et al. because Klogether et al. and Loschmann et al. demonstrated that an AMPA receptor antagonist *potentiates* the effects of a dopamine agonist in animal models of bradykinesia.

This is *not* persuasive because the relationship, and therefore the relevance of bradykinesia to dopamine-induced dyskinesia is not explained. It is possible that because dyskinesia is a hyperkinetic movement disorder, while bradykinesia is a hypokinetic movement disorder, one of ordinary skill in the art would have had a reasonable expectation that AMPA receptor antagonists might have an opposite effects on two responses that were opposite in nature, *i.e.,* because AMPA receptor antagonists increase bradykinesia such antagonists might reasonably be expected to decrease dyskinesia. Therefore the showing is taken as not persuasive and not relevant.

New Claim Rejections

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3 and 5-7 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a *Written Description* rejection.

The claims are drawn to AMPA receptor antagonist effective in treating dyskinesia associated with dopamine agonist therapy in a mammal. The claims do not require that the AMPA receptor antagonist possess any particular conserved structure, or other distinguishing feature. Thus, the claims are drawn to a genus of receptor antagonist defined by the ability to treat dyskinesia induced by dopamine agonist therapy.

The specification at p. 1, states that AMPA receptors mediate fast excitatory transmission throughout the brain, including areas in movement and that "[b]y inhibiting the AMPA receptor through administration of an AMPA receptor antagonist, dyskinesias associated with dopamine agonist therapy may be treated in accord with the present invention as described below." The specification at pp. 2-3 provide patents wherein

AMPA receptor antagonists are referred to. The specification at p. 10, Example 1, provide a working example of *in vivo* experimental reduction of L-Dopa-induced dyskinesias by administering the AMPA receptor antagonist 3-(2-chloro-phenyl)-2-[2-(6-diethylaminomethyl-pyridin-2-yl)-vinyl]-6-fluoro-3-H-quinazolin-4-one to monkeys.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and / or chemical properties, functional characteristics, structure / function correlation, methods of making the claimed product, and any combination thereof. In this case, the only AMPA receptor antagonist present in the claims is the AMPA receptor antagonist 3-(2-chloro-phenyl)-2-[2-(6-diethylaminomethyl-pyridin-2-yl)-vinyl]-6-fluoro-3-H-quinazolin-4-one. The specification does not identify any particular portion of that structure or any other structure that must be conserved, nor does it provide a disclosure of any structure / function correlation to specifically treat dyskinesias induced by dopamine agonist therapy. The specification does not provide description of specific AMPA receptor antagonists that would not treat other dyskinesias, such as tardive dyskinesia. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See Vas-Cath at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of AMPA receptor antagonists capable of specifically treating dyskinesia associated with dopamine agonist therapy in a mammal, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of treatment. Adequate written description requires more than a mere statement that the genus of AMPA receptor antagonists is part of the invention and reference to a potential method of treatment of L-Dopa-induced dyskinesia. The compounds themselves are required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the AMPA receptor antagonist 3-(2-chloro-phenyl)-2-[2-(6-diethylaminomethyl-pyridin-2-yl)-vinyl]-6-fluoro-3-H-quinazolin-4-one, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 § 112 is severable from its enablement provision.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "said compound" in line 1. There is no antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the

examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

9. Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Arnold et al.** (US 5,670,516), **Gerlach** (Danish Medical Bulletin, 1979 26/5 pp. 209-245) and **Adams et al.** (Principles of Neurology, on PTO-1449).

Arnold et al. teach a number of neurological disorders such as "drug-induced Parkinson's Disease" and other neurological conditions such as "muscular spasms" and tardive dyskinesia" (see column 1, line 55 through column 2, line 4). The reference teaches that the "use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders" (column 2, lines 4-9).

Arnold et al. do not teach the using of an AMPA receptor antagonist to "treat dyskinesia associated with dopamine agonist therapy."

Gerlach teaches:

> L-Dopa-induced hyperkinesias in Parkinson patients may likewise be indistinguishable from TD [tardive dyskinesia], although L-Dopa-induced hyperkinesias involves head and extremities to a higher degree (see Fig. 5).
>
> These . . . hyperkinetic syndromes represent obvious clinical analogues to TD and can . . . serve to elucidate TD.

Gerlach, at p. 215, para 3.2.1.

Adams et al. state that one of the "most common and troublesome effects of L-dopa" is dyskinesia (see page 1073, col. 1, 2nd full paragraph. Furthermore, Adams et al. teach the combination of L-dopa with a decarboxylase inhibitor (carbidopa or

benserazide) which is standard L-dopa therapy and reads on the limitations of the instant claims 2, 3, 6, and 7. See page 1072 of Adams et al., 2nd column, 3rd paragraph.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use an AMPA receptor antagonist (as taught by Arnold et al.) to treat dyskinesia associated with dopamine agonist therapy for the following reasons. Adams et al. teach that one of the "most common and troublesome effects of L-dopa" is dyskinesia. Arnold et al. teach a number of neurological conditions such as "muscular spasms" and "tardive dyskinesia" that can be treated using an AMPA receptor antagonist. Gerlach teaches that L-Dopa-induced hyperkinesias is indistinguishable from tardive dyskinesia and represents an obvious clinical analogue to tardive dyskinesia.

One of ordinary skill in the art would have been motivated to use an AMPA receptor antagonist to treat dyskinesia associated with dopamine agonist therapy because Arnold et al. teach that blocking AMPA receptors is an effective way to treat neurological disorders, such as tardive dyskinesia, Gerlach teaches that L-Dopa-induced hyperkinesia is indistinguishable from tardive dyskinesia, and Adams et al. teach that one of the "most common and troublesome effects of L-dopa is dyskinesia." One of ordinary skill in the art would have been motivated to administer an AMPA receptor antagonist in patients treated with L-dopa and to offset the effects caused by the dopamine agonist therapy because Arnold teaches using such antagonists to treat tardive dyskinesia and Gerlach teaches L-Dopa-induced dyskinesia to be an obvious clinical analogue to tardive dyskinesia.

Conclusion

10. Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark Shibuya
Examiner
Art Unit 1639

PADMASHRI PONNALURI
PRIMARY EXAMINER

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